TB Grand Rounds

Unusual Presentations of TB

Amanuel Rosario, MD & Diana Nilsen, MD
April 24, 2007

Speaker: Amanuel Rosario, MD

- Medical Director of the District of Columbia TB Control Program
- Infectious diseases (HIV) specialist
**Patient History**

- 26 y/o African American female admitted to hospital (on 3/29/06) for fever, weight loss x3 months, cough and hemoptysis
- Past medical history significant for sickel cell trait, iron def. anemia

**Social History**

- No history of travel to endemic area
- No history of recent known TB contact
- Employed at Home Depot
- Single and lives in apartment alone
- Uses marijuana occasionally and drinks alcohol socially
Physical Exam (on initial clinic visit)

- Temp 99, wt. 156lbs, BP 101/61, RR 22/min, Pulse 104/min
- Well developed, appeared ill
- HEENT: unremarkable
- LN: no cervical or axillary lymphadenopathy
- Neck: supple
- Lungs: clear to auscultation
- CVS: tachycardia
- Abdomen: soft nontender, no organomegally
- Skin: no rash
- CNS: alert, oriented x3; cranial nerves ii-xii intact; no focal deficit

Radiographic Findings: CXR

- CXR (3/29/06):
  - Right paratracheal, right hilar adenopathy. Very fine nodular pattern (bilaterally)
Radiographic Findings: CT

- CT of chest with contrast (3/31/06):
  - Mediastinal and hilar adenopathy with multiple tiny interstitial nodules with miliary pattern
  - Suspicious for tuberculosis

Questions & Points for Clarification
**Working Diagnosis**

- Suspected pulmonary and extra-pulmonary (mediastinal LN) TB

**Laboratory Results**

- 4/12/06

<table>
<thead>
<tr>
<th>CBC</th>
<th>LFTs</th>
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<tbody>
<tr>
<td>WBC 6.3</td>
<td>Ast 76</td>
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<tr>
<td>HGB 9.7</td>
<td>Alt 36</td>
</tr>
<tr>
<td>HCT 26.9</td>
<td>Alp 165</td>
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<tr>
<td>PLT 415</td>
<td>Alb 3.1</td>
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<tr>
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<td>TB 1.2</td>
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<td>Creatinine 0.6</td>
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- Tuberculin skin test negative
- 5/31/06 – HIV test non-reactive
Laboratory Results Cont’d

- On 4/6/06
  - Biopsy of mediastinal LN revealed caseating and non-caseating granuloma
  - AFB stain positive

Treatment Course

- 4/8/06: started on treatment with INH, RIF, EMB, PZA
  - Initial phase with INH, RIF, EMB, PZA from 4/8/06 – 6/8/06
  - Continuation phase with INH and RIF from 6/8/06 until present
- On directly observed therapy (DOT)
Treatment Course Cont’d

- 10 weeks after starting anti-TB treatment (6/17/06), patient developed multiple skin nodules and reported 1 episode of seizures

Interpretation of findings and other considerations
**Treatment Course Cont’d**

- Patient was evaluated at NIH
  - MRI of brain
  - Skin biopsy (superficial and deep) path-microabscesses
  - Anti-TB meds continued
- MRI of brain (9/13/06):
  - Multiple complex rim enhancing lesions at right frontal lobe, midbrain. No patchy meningeal enhancement

**Interpretation of MRI findings**
**Bacteriology**

<table>
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<tr>
<th>Date</th>
<th>Source</th>
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<th>Culture</th>
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<td>LN bx</td>
<td>Neg.</td>
<td><em>M. tb</em></td>
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<td>4/11/06</td>
<td>Sputum</td>
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<td><em>M. tb</em></td>
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<td>Sputum</td>
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<td>8/14/06</td>
<td>Skin bx</td>
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**Drug susceptibility studies: Pan sensitive**

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**Treatment Course Cont’d**

- Despite these findings, no changes in her treatment were initiated
  - Patient continued to improve clinically
  - Symptoms resolved
  - Weight gain of more than 20 lbs
  - Skin nodules resolved
  - Smear and culture results remained negative at this point


Discussion

- Patient developed multiple skin lesions (nodules) and CNS lesion c/w tuberculoma after starting anti-TB therapy
- Despite these findings, patient continued to clinically improve with dramatic improvement in symptoms, and weight gain of more than 20 lbs
- This clinical syndrome appears most consistent with paradoxical response to TB therapy
  - New site may exhibit signs and symptoms of infection, commonly CNS and skin lesions
  - Many cases have been described in medical literature
Paradoxical Response (PR) during TB Treatment

- Deterioration during anti-TB therapy remains a clinical challenge
- PR is defined as clinical or radiological worsening of previous tuberculous lesions or the development of new lesions in a patient who initially improves with anti-therapy
- Various series suggest that PR are not a rare phenomenon, identified in 6-30% of patients receiving TB therapy

Campbell et al. Tubercle 1977;58:171-179

Clinical Spectrum of PR

- Review 122 episodes of PR in HIV-negative patients after anti-TB therapy demonstrated:
  - High propensity for CNS involvement (appearance of intracranial tuberculomas) described in almost 50% of all cases reported in literature
  - In contrast, findings among HIV-infected patients (57 episodes of PR) only 3.5% demonstrated new tuberculomas
Clinical Spectrum of PR

- Second most commonly reported manifestation was pleural involvement (pleural effusion)
- Other superficial sites include:
  - Peripheral lymph node involvement (4%) in this series was less common than in HIV-positive patients (41%)
  - Skin and soft tissues and bone and tendons involvement are also occasionally observed

Presentation of PR

- Patients with pulmonary, pleural, miliary, and lymph node TB could develop intracranial tuberculomas between 2 wks and 3 mos after initiation of anti-TB therapy
- Similarly, the appearance of pleural effusion could occur after 3-19 wks of anti-TB therapy
Treatment of PR

- Surgical interventions (60.7%)
  - Insertion of VP shunt, resection of intracranial lesions, percutaneous drainage of pleural effusion, excision of enlarged lymph nodes and subcutaneous abscesses
- Changes in TB treatment regimen (15.6%)
- Conservative management/continuation of original therapy (13.9%)
- Steroid use appeared to be safe in this series (39.3%)
  

Treatment of PR

- Non severe paradoxical reactions
  - Treat symptomatically without change in anti-TB therapy
- Severe reactions (i.e., high fever, airway compromised from enlarging lymph nodes, enlarging serosal fluid collections, sepsis syndrome)
  - Approaches to management of severe reactions have not been studied
  - Expert opinion suggests prednisone or methylprednisolone starting at 1mg/kg and gradually reduced after 1 to 2 wks

MMWR 2003; 52 (No. RR-11)
**PR in HIV-coinfected patients**

- The early introduction of HAART and the presence of disseminated TB are associated with the development of PR in HIV/TB patients


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**Results of CT & MRI**

- **CT Scan of Chest (2/22/07):**
  - Stable mediastinal adenopathy; tiny pulmonary nodules no longer visible

- **MRI of brain (2/22/07):**
  - No new lesion, no evidence of progression, some minimal reduction in size
Questions

- How long should we treat the patient?
- What parameter should be used to assess response?
- How frequent should we follow with neuroimaging?

Speaker: Diana Nilsen, MD

- Director of Medical Affairs, Bureau of TB Control at NYC Dept. of Health & Mental Hygiene
- Oversees care of TB patients at 10 Bureau of TB Chest Centers
- Supervises medical consultants who review TB cases in the field
History of Present Illness

• 24 y/o female originally born in Tibet, who moved to India age 6
• She emigrated to US in 2000
• Patient presented to Bureau of TB Control Chest Center (BTBC) on 5/11/06 with complaints of:
  – Cough for 1 year
  – Waxing/waning fever and fatigue
  – 2 episodes of hemoptysis

Past Medical History

• 10/05: patient was seen by PMD and given Tequin with some improvement
• CXR/CT scan were performed in 4/06
• PMD concerned patient has sarcoid
• No other significant PMH except:
  – Patient was seen at a BTBC clinic in 2002 with positive TST (14 mm) and negative CXR
  – Patient refused LTBI treatment at that time
Social History

- Patient is smoker (4-5 cigs/day)
- No ETOH use
- HIV negative (12/05)
- Employed as cashier at gourmet food store

Physical Exam

- Temp 99, BP 90/70, HR 70, RR 14, Wt 140 lbs
- Well-appearing female
- No lymphadenopathy
- Throat - clear
- Lungs - clear without wheezes, rales
- Abdomen - soft non-tender, not distended
What would you do?
Bacteriology

- Three sputum specimens were collected for AFB – 5/11, 5/12, 5/13
- Amplified Mycobacterium Tuberculosis Direct Test (MTD) performed on 5/12 and 5/13 specimen

Presentation

- Patient seen by BTBC chest physician on 5/15 (4 days after initial visit)
- Forgot to mention a new “lesion” on her foot
- Warm, fluctuant 3cm x 3cm mass with surrounding erythema
Plan

- Send patient to referral hospital for evaluation for bronchoscopy on 5/18 unless smears return positive
- Asked to retrieve 4/06 Chest CT scan from private outpatient radiology center

CT – 4/06
Further Evaluation

- Three sputum smears negative for AFB and MTD tests were negative
- While at referral hospital for evaluation for bronchoscopy:
  - Left foot was aspirated and sent for AFB
  - X-ray of left foot showed no evidence of bony involvement; soft tissue swelling of lateral aspect of the foot
Bronchoscopy Results

- BAL - No acid fast bacilli, no herpes or CMV
- Transbronchial biopsy path showed – non-necrotizing granulomatous inflammation with fibrosis
  – negative for malignancy, AFB

What is the Differential Diagnosis?

- Lymphoma
- Nontuberculous mycobacteria
- M.tb
- Sarcoidosis
- Eosinophilic granuloma (Histiocytosis X)
- Fungal infection
What is your next step?

Next step?

- Open lung biopsy
- Empirically start TB meds (IRPE)
- Wait for further special stains to rule out eosinophilic granuloma
- Start steroids??
Follow-up

• Special stains negative for eosinophilic granuloma
• Patient started on TB meds on 6/1 with IRPE
• Phone call from referral hospital 6/5/06 - Aspirate from foot - growing *M.tb*
Follow up (cont.)

- Sputum’s from 5/12 and 5/13 culture grew *M. tuberculosis* complex
- Pansensitive isolate!!
- Patient started on IRPE
- Completed 9 months of treatment with no complications on DOT

Questions, Comments & Discussion